FINNISH CARDIAC SOCIETY

51st Progress Report Meeting

April 2, 2025, Turku

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51st Progress Report Meeting Programme

Teatro-sali. Session 1. 51st Progress Report Meeting – Young Investigators Award Competition

Chairperson Marja Hedman, Finnish Cardiac Society

Meeting is supported by unrestricted educational grant from Boehringer Ingelheim

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History of the Progress Report Meetings

Progress Report Meeting is organized by Finnish Cardiac Society to present opportunity for young investigators to report results of their studies. An important point is also training in presenting scientific papers to criticism of senior colleagues.

Boehringer Ingelheim has supported organizing the meeting from the beginning, 1975 by helping in practical matters and presenting grants to the best of speakers.

Winners of the Boehringer Ingelheim grants

From year 2007 onwards the competition has had two categories instead of 1st and 2nd prize. However, if less than three eligible abstracts have been received to either category, the organizers reserve the right to combine the categories.

Year	1st Prize	2nd Prize
1975	Erkki Pesonen	–
1976	Heikki Karppanen	Markku S. Nieminen
1977	Matti Halinen	Ulla Korhonen
1978	Ilkka Torstila	Markku S. Nieminen
1979	Olli Meretoja	Aila Rissanen
1980	Jorma Viikari	Jouko Jalonen
1981	Markku Kupari	Irma Koivula
1982	Heikki Huikuri	Markku Kupari
1983	Seppo Hietakorpi	Kari Niemelä
1984	Markku Laakso	Heikki Huikuri
1985	Jukka Räisänen	Kari Niemelä
1986	Pekka Koskinen	Juha Mustonen
1987	Kimmo Mattila	Silja Majahalme
1988	Heikki Tikkanen	Paula Rämö
1989	Hannu Näveri	Keijo Peuhkurinen
1990	Markku Mäkijärvi	Juhani Valkama
1991	Eero Mervaala	Paavo Uusimaa
1992	Eero Mervaala	Anne Remes
1993	Juha Hartikainen	Helena Kovanen
1994	Kai Kiilavuori	Juha Perkiömäki
1995	Sirkku Pikkujämsä	Pasi Tavi
1996	Jorma Kokkonen	Timo Mäkikallio
1997	Pekka Raatikainen	Marja Laitinen
1998	Marja Laitinen	Antti Ylitalo, 3rd Prize Timo Mäkikallio
1999	Mika Laine	Timo Mäkikallio
2000	Saila Vikman	Antti Kivelä
2001	Jari Tapanainen	Pertti Jääskeläinen
2002	Tuomas Rissanen	Markku Pentikäinen
2003	Juhani Junttila	Markus Leskinen
2004	Jere Paavola	Tuomas Rissanen
2005	Mikko Mäyränpää	Satu Helske
2006	Olli Tenhunen	Johan Lassus

Year	Basic Science category	Clinical Research category
2007	Satu Helske	Ville Kytö
2008	Mirella Hietaniemi	Minna Kylmälä
2009	Johanna Lähteenvuo o.s. Markkanen	Annukka Marjamaa
2010	1st Prize Jani Tikkanen 2nd Prize Riina Kandolin	the categories were combined
2011	Markku Lähteenvuo	Aapo Aro
2012	1st Prize Kirsi Kujala 2nd Prize Maija Bry	the categories were combined
2013	Suvi Syväranta	Toni Grönberg
2014	1st Prize Leena Kaikkonen 2nd Prize Heli Tolppanen	the categories were combined
2015	1st Prize Aissa Bah 1st Prize Markus Räsänen	the categories were combined
2016	1st Prize Heli Tolppanen 1st Prize Kaj Ekström	the categories were combined
2017	Tarja Alakoski	Samuli Jaakkola
2018	Maija Ruuth	Tero Penttilä
2019	Annakaisa Tirronen	Anette Haukilahti
2020	1st Prize, Tiia Istolahti 1st Prize, Henna Korpela 2nd Prize, Vilbert Sikorski	the categories were combined
2021	1st Prize Aleksi Leikas 2nd Prize Minna Koivunen	the categories were combined
2022	1st Prize Markus Ritvos 2nd Prize Kristiina Harju	the categories were combined
2023	1st Prize Anne Doedens 2nd Prize Valtteri Muroke	the categories were combined
2024	1st Prize Marko Taipale 2nd Prize Lauri Äikäs	the categories were combined

Presentation time
11.25–11.35

MD Marko Vilpponen
University of Helsinki, Finland

Clinical characteristics associated with not using oral anticoagulants at the time of first ischemic stroke in patients with atrial fibrillation: a nationwide study

Marko Vilpponen, University of Helsinki, Finland, Aapo Aro, Heart and Lung Center, Helsinki University Hospital and University of Helsinki, Olli Halminen, Department of Industrial Engineering and Management, Aalto University, Espoo, Finland, Paula Tiili, Primary Health Care Unit, Helsinki University Hospital, Helsinki, Finland; Mika Linna, Department of Industrial Engineering and Management, Aalto University, Espoo, Finland, Alex Luojus, University of Helsinki, Finland; Konsta Teppo, Heart Center, Turku University Hospital and University of Turku, Finland; Pirjo Mustonen, Heart Center, Turku University Hospital and University of Turku, Finland; Jari Haukka, Department of Public Health, University of Helsinki, Finland; Juha Hartikainen, Heart Center, Kuopio University Hospital and University of Eastern Finland, Kuopio; Juhani Airaksinen, Heart Center, Turku University Hospital and University of Turku, Finland; Mika Lehto, Department of Internal Medicine, Jorvi Hospital and Helsinki University Hospital; Jukka Putaala, Department of Neurology, Helsinki University Hospital and University of Helsinki

Background

Limited data exist on characteristics and patterns associated with patients with atrial fibrillation (AF) who encounter first-ever ischemic stroke (IS) while not on oral anticoagulation (OAC) therapy.

Methods

From a nationwide registry-linkage database including all patients with AF in Finland from 2007 to 2017, we included those with IS >90 days after diagnosis of AF and those without IS. Factors associated with non-OAC use among IS patients were examined using logistic regression, with separate models for independent variables and risk scores.

Results

Among 174 092 patients with new-onset AF, 9635 (5.5%) patients (56.8% female; mean age 79.2 years) experienced IS >90 days after AF diagnosis. A total of 6021 (62.5%) of IS patients were not on OAC at the time of IS (mean age 79.0 years; 57.1% female). The proportion of non-OAC decreased from 67.0% to 49.5% over the study period. In the adjusted logistic regression model, the strongest factor associated with non-OAC was CHA2DS2-VA score of 0 points (OR 7.056, [95%CI, 4.441–11.211)], followed by a score of 1 point (OR 3.035 [95% CI, 2.448–3.762]). Other significant independent factors associated with non-OAC use were alcohol abuse (OR 2.218 [95% CI, 1.759–2.796)], liver dysfunction (OR 1.922 [95% CI, 1.223–3.022]), age < 65 years (OR 1.838 [95% CI, 1.552–2.176)], renal dysfunction (OR 1.410 [95% CI, 1.171–1.698)], dementia (OR 1.410 [95% CI, 1.232–1.614)], antiplatelets/NSAID use (OR 1.293 [95% CI, 1.185–1.411)], prior myocardial infarction (OR 1.250 [95% CI, 1.085–1.438]), female sex (OR 1.194 [95% CI, 1.087–1.312]) and lowest income (OR 1.152 [95% CI, 1.011–1.312]). As part of a secondary analysis, 8818 IS patients (91.5% of all IS patients) had a CHA_2DS_2-VA score of ≥2 (mean age 80.9 years, 59.0% female, mean follow-up 3.3 years). Of the 9635 patients, 1565 (16.2%) died within 30 days of the IS event.

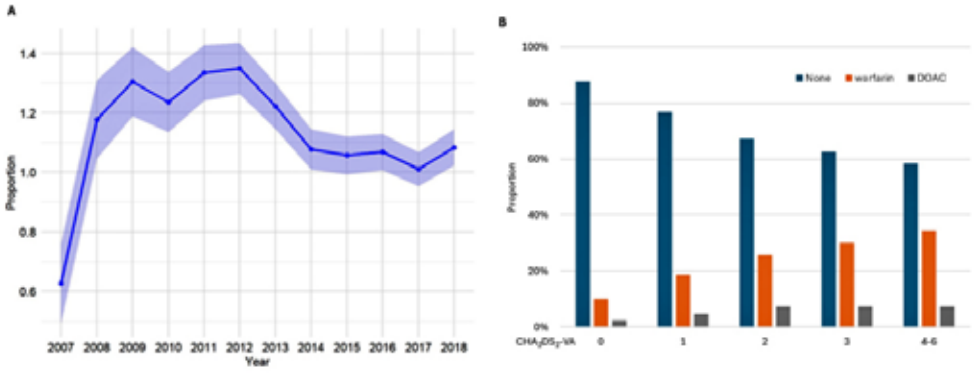
Conclusions

A significant proportion of high-risk AF patients experiencing IS were without appropriate OAC therapy at the time of the event. However, decreasing trend of non-OAC use was identified throughout the study period.

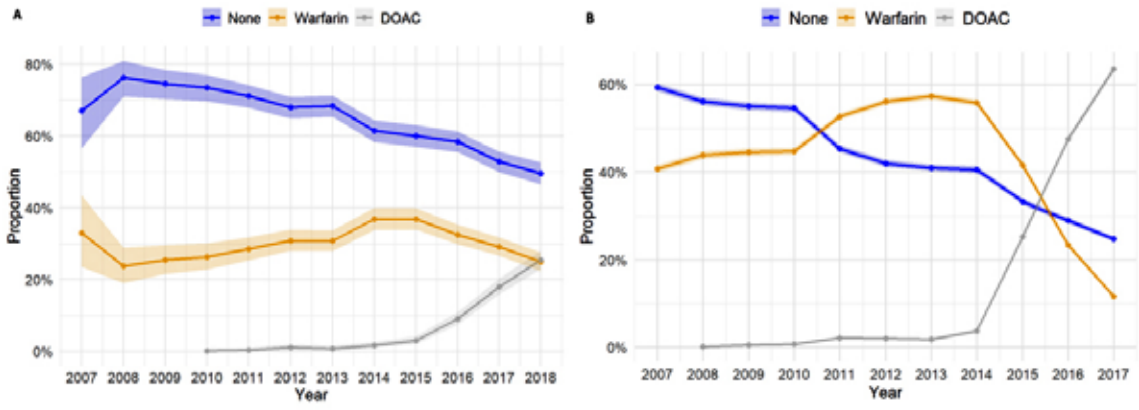
Presentation time
11.25–11.35

MD Marko Vilpponen
University of Helsinki, Finland

A. Proportion of first-ever ischemic stroke events occurring >90 days after incident atrial fibrillation, by calendar year, among patients at risk; cumulatively excluding those with prior stroke or death, with 95% confidence intervals. **B,** Proportion of oral anticoagulation purchases according to CHA_2DS_2-VA score in first-ever ischemic stroke patients > 90 days since AF diagnosis.



A, Annual proportion of oral anticoagulation purchases in first-ever ischemic stroke patients > 90 days since AF diagnosis, with Clopper-Pearson 95% confidence intervals. **B,** Annual proportion of oral anticoagulation purchases in AF patients without stroke, with Clopper-Pearson 95% confidence intervals.



Presentation time
11.35–11.45

PhD Candidate Yi Li
University of Oulu

Visualization and quantification of the atrioventricular conduction axis using quantitative magnetic resonance imaging

Yi Li, University of Oulu, Timo Liimatainen, University of Oulu

Introduction

The atrioventricular conduction axis (AVCA) consists of the bundle of His and atrioventricular node (AVN). AVCA transmits electrical impulses from the atria to the ventricles. The recent upsurge of His-bundle pacing has emphasized the need for visualization the arrangement of AVCA. The AVN is insulated from myocardium by the central fibrous body (CFB), which may offer potential for visualization. The aim of this study was to identify the AVCA structure using non-invasive rotating-frame relaxation-time mappings (TRAFF2 and T1ρ) in ex vivo swine hearts.

Methods

Tissue blocks (n=5) including AVN and bundle of His were scanned on a 3 T clinical MRI system. The imaging sequences for comparison are TRAFF2, T1ρ, T2, T1. The nominal power for TRAFF2, T1ρ is 500Hz. Histological sections at three levels were stained with Masson's Trichrome. Blue channel of the histology images was used for analyses. Regions of interests (ROIs) of myocardium, AVCA and CFB were chosen using multi-Otsu thresholding. The contrast was defined by relative relaxation time difference, RRTD=2[T(AVCA)-T(myocardium)]/[T(AVCA)+T(myocardium)] (T = average relaxation time). Differences in relaxation times were compared by Student's t-test with Benjamini-Hochberg correction. Pearson correlations between ROIs in the relaxation time maps and histology were computed.

Results/Discussions

Increased relaxation time in the AVCA compared to myocardium area was shown in the maps (Figure 1). The histology images covering bundle of His and compact AVN validated the locations of the MRI ROIs (Figure 1). The SAN structure can be delineated with higher relaxation time in 3D reconstructed TRAFF2 map (Figure 1). Significant differences between AVCA and myocardium areas were found in all relaxation times (Figure 2A). RRTDs in TRAFF2 and T1ρ were significantly higher than in T2 and T1. TRAFF2, T1ρ and T2 in myocardium, AVCA and CFB showed a significant correlation with histology (Figure 2 B-C). Relaxation times in ROIs were highly correlated with histology blue channel signal based on the fibrous content. Our results align with previous studies, which show elevated TRAFF2 and T1ρ in myocardial infarcts (high fibrotic content) compared to remote myocardium areas.

Conclusions

The AVCA components can be visualized and quantitated in the TRAFF2 and T1ρ. The relaxation times in different parts of AVCA are correlated significantly with corresponding histology, based on variation in fibrotic content. TRAFF2 and T1ρ maps are feasible non-invasive contrast-agent free imaging methods for visualizing the bundle of His and AVN in ex vivo swine heart.

Presentation time
11.35–11.45

PhD Candidate Yi Li
University of Oulu

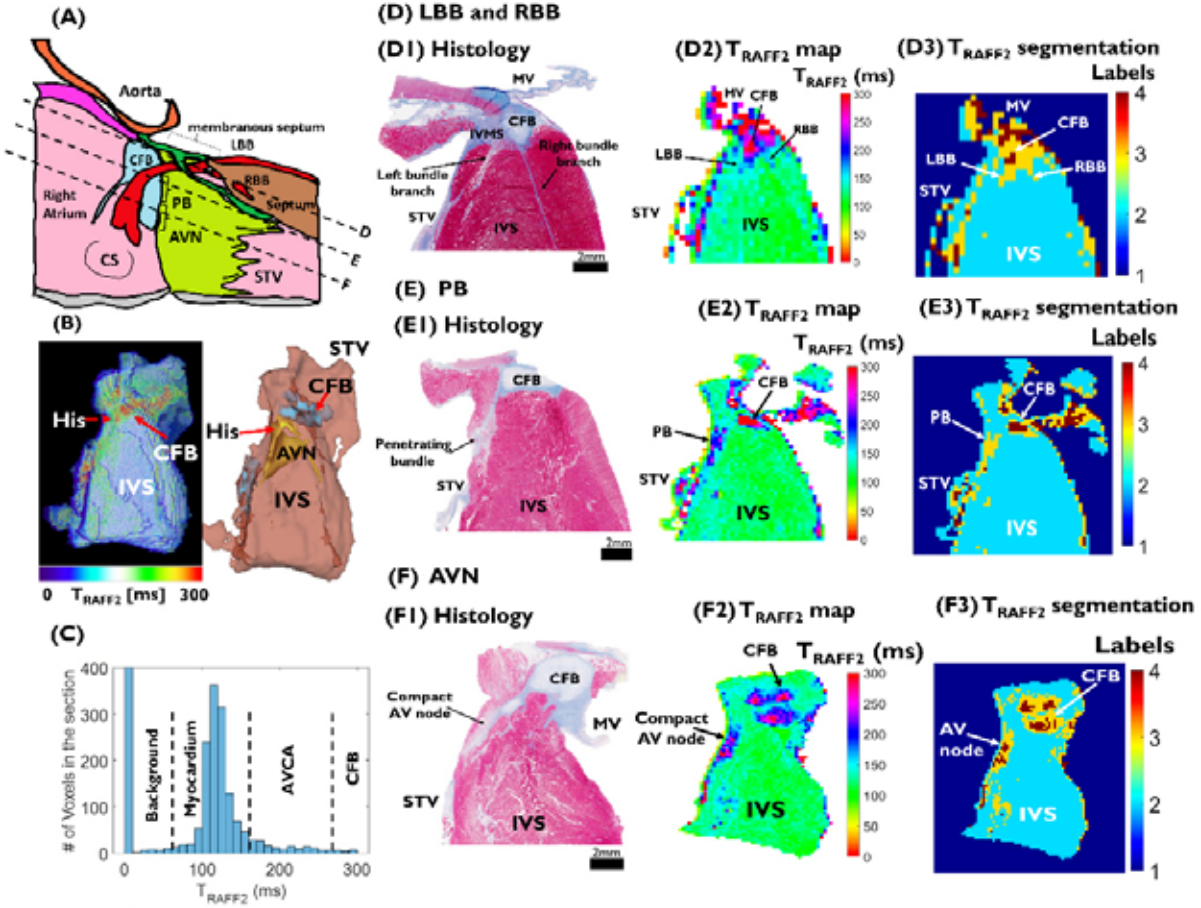


Figure 1

(A) Schematic of AVCA. The black dashed lines D, E, F, G show the different levels of the histological sections.
(B) 3D T_{RAFF2} map and segmentation results in 3D reconstructed structure.
(C) Histogram to show the threshold for segmentation (multi-Otsu thresholding).
(D1-G1) The Masson's trichrome stained histology sections at four levels from branching bundles to the compact AV node. (D2-G2) The corresponding TRAFF2 maps at four levels. (D3-G3) Segmentation of AVCA in TRAFF2 maps. Masson's trichrome stain coloring myocardium in red and fibrous tissue in blue/green.
CFB, central fibrotic body; CS, coronary sinus; IVS, interventricular septum; LBB (RBB), left (right) bundle branch; PB, penetrating bundle; STV, septal leaflet of the tricuspid valve.

PhD Candidate Yi Li
University of Oulu

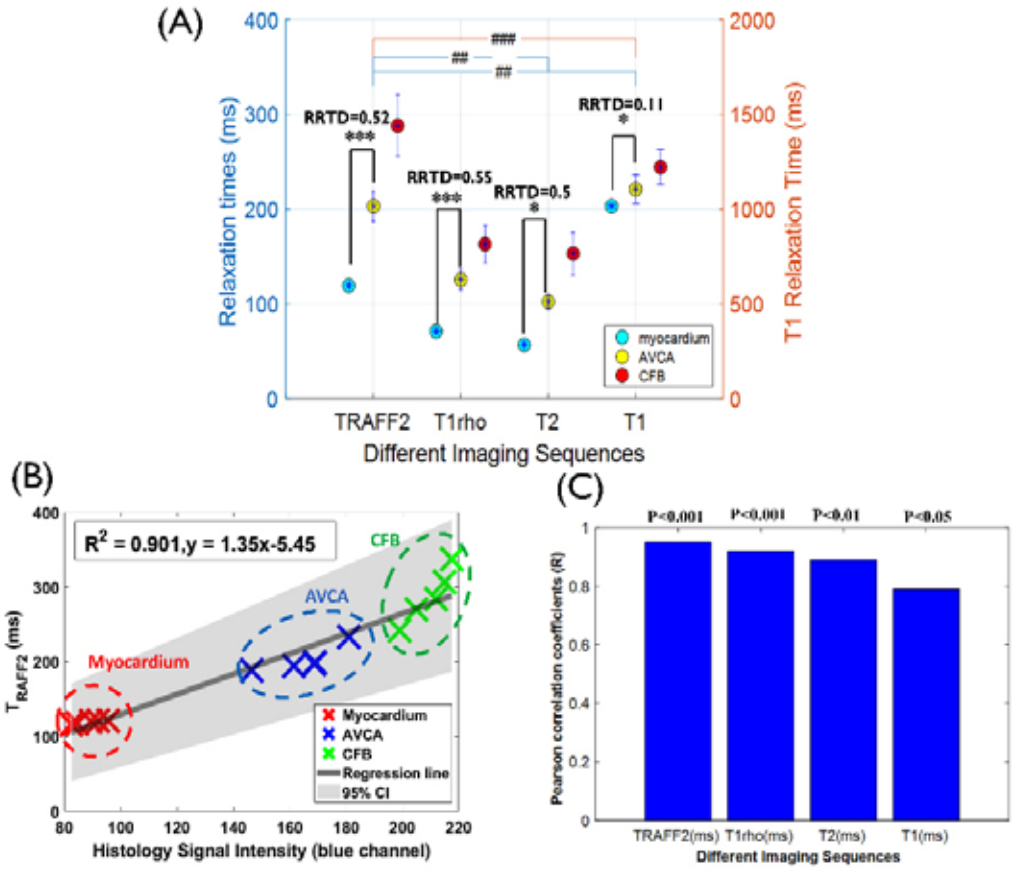


Figure 2

(A) Relaxation times for myocardium, AVCA and CFB. *P<0.05, ***P<0.001 for differences in the relaxation time between AVCA and myocardium; and ##P<0.01, ###P<0.001 for differences in the contrast using T_{RAFF2} as the reference.

(B) Linear correlation between T_{RAFF2} and the blue component of Masson's trichrome stained histology sections, derived from myocardium, AVCA and CFB ROI averages.

(C) Pearson correlation coefficients (R) between the relaxation time maps and signal intensity of blue channel in the histology images with significant level P.

Presentation time
11.45–11.55

PhD Candidate, MSc Imran Iqbal
Turku PET Centre, University of Turku

Evaluation of [18F]FOL, a PET tracer targeting folate receptor-β-expressing macrophages, to image immune response and predict left ventricular function in experimental myocardial infarction

Imran Iqbal, Turku PET Centre, University of Turku, Heidi Liljenbäck, Turku PET Centre, University of Turku and Turku University Hospital; Putri Andriana, Turku PET Centre, University of Turku and Turku University Hospital; Mia Ståhle, Turku PET Centre, University of Turku and Turku University Hospital; Jenni Virta, Turku PET Centre, University of Turku and Turku University Hospital; Erika Atencio Herre, Turku PET Centre, University of Turku and Turku University Hospital; Maxwell WG Miner, Turku PET Centre, University of Turku and Turku University Hospital; Arman Anand, Turku PET Centre, University of Turku and Turku University Hospital; Aino Suni, Turku PET Centre, University of Turku and Turku University Hospital; Wail Nammas, Turku PET Centre, University of Turku and Turku University Hospital; Ville Kytö, Turku PET Centre, University of Turku and Turku University Hospital; Hasan Mansour A Mansour, Department of Chemistry, Purdue University; Nathan A Cleaveland, Department of Chemistry, Purdue University; Xiang-Guo Li, Turku PET Centre, University of Turku and Turku University Hospital; Madduri Srinivasarao, Department of Chemistry, Purdue University; Philip S. Low, Department of Chemistry, Purdue University; Juhani Knuuti, Turku PET Centre, University of Turku and Turku University Hospital; Anne Roivainen, Turku PET Centre, University of Turku and Turku University Hospital; Antti Saraste, Turku PET Centre, University of Turku and Turku University Hospital

Aim

Aluminium fluoride-18-labeled 1,4,7,-triazacylononane-1,4,7-triacetic acid conjugated folate ([18F]FOL) is a positron emission tomography (PET) tracer that targets folate receptor-β (FR-β) expressed on activated macrophages. We evaluated [18F]FOL for imaging immune response in a rat model of myocardial infarction (MI).

Methods

Rats underwent surgical ligation of the left coronary artery (LCA) to induce MI or sham-operation. [18F]FOL PET was performed on days 3, 7, 15, and 90 post-surgery. [18F]FDG PET was performed in order to localize myocardium and area of MI. Autoradiography ([18F]FOL uptake), staining of CD68 (macrophages), and staining of FR-ß were performed on myocardial tissue sections. A subgroup of rats (n=15) underwent [18F]FOL PET and serial echocardiography in order to monitor left ventricular (LV) function.

Results

The presence of MI was confirmed by histology. PET images showed significantly higher uptake of [18F]FOL ($p<0.001$) in the infarct area compared to sham area on day 3 (SUV 1.97±0.17 vs. 0.74±0.13), day 7 (SUV 1.35±0.33 vs. 0.70±0.16), day 15 (SUV 1.24±0.20 vs. 0.59±0.07), and day 90 (SUV 1.39±0.25 vs. 0.69±0.11). On day 3, pre-administration of folate glucosamine (n=3) reduced the [18F]FOL signal by 52% in the infarct area indicating specific binding to FR-β. Autoradiography confirmed increased uptake of [18F]FOL in the MI area. Immunofluorescence microscopy showed FR-ß-expression in CD68-positive macrophages in the infarct area. A positive correlation was observed between [18F]FOL uptake on PET images and the areal percentage of CD68-positivity in the infarct area ($r=0.669$, $p<0.001$). [18F]FOL uptake on day 7 post-MI was associated with decline in LV ejection fraction ($r=-0.665$, $p<0.007$) between days 7 and 90 post-MI.

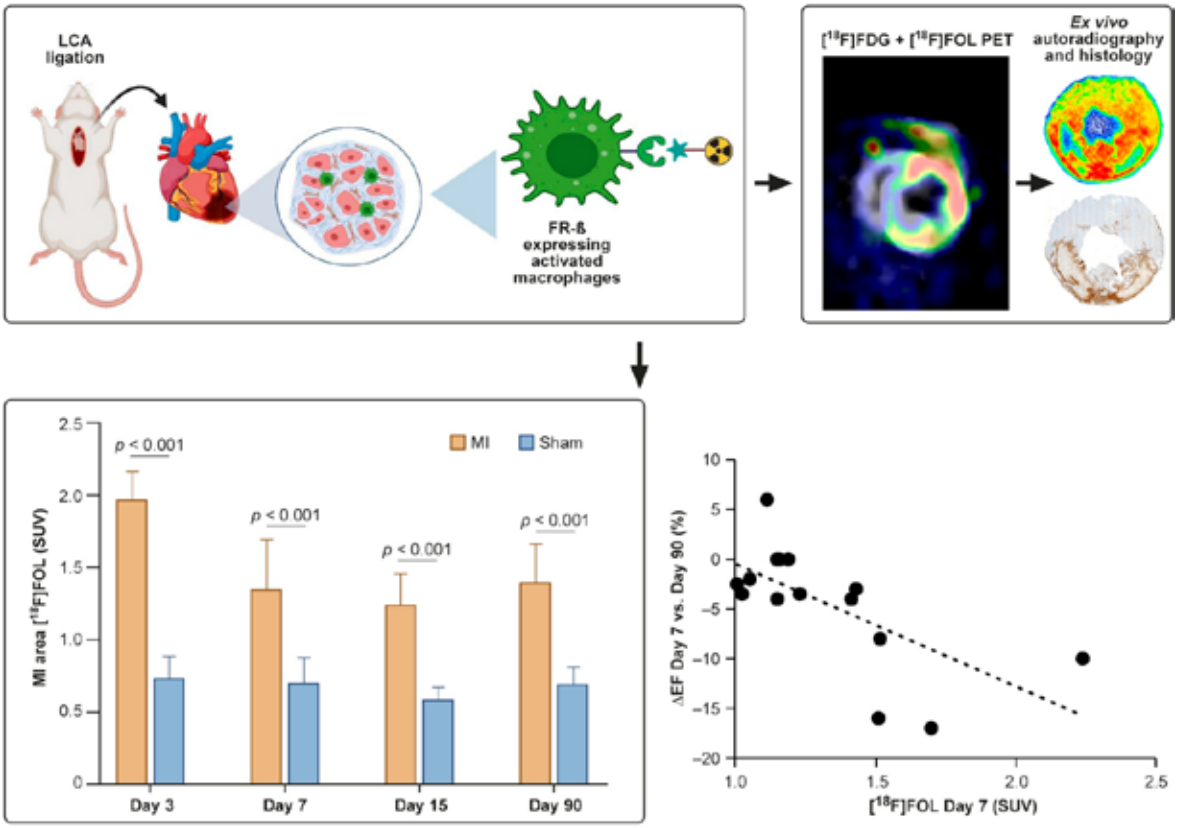
Presentation time
11.45–11.55

PhD Candidate, MSc Imran Iqbal
Turku PET Centre, University of Turku

Conclusions

Cardiac [18F]FOL PET detects FR-ß-expressing macrophages associated with active inflammation post-MI. The uptake of [18F]FOL peaks early and remains elevated up to 3 months in the infarct area. Increased [18F]FOL uptake early post-MI is associated with worsening of LV function late post-MI.

Key Words: Macrophages, Folate receptor beta, PET, [18F]FOL, myocardial infarction, heart failure.



Presentation time
11.55–12.05

MSc Anna Kemppi
University of Oulu

Sprouty-1 regulates fibroblast function and development of myocardial fibrosis

Anna Kemppi, University of Oulu, Tarja Alakoski, University of Oulu; Tuomo Huotari, University of Oulu; Lea Rahtu-Korpela, University of Oulu; Samu Saarimäki, University of Oulu; Sini Skarp, University of Oulu; Zoltan Szabo, University of Oulu; Johanna Magga, University of Oulu; Risto Kerkelä, University of Oulu

Myocardial fibrosis is one of the key pathological features of cardiovascular diseases, contributing to impaired cardiac function, adverse remodeling and predisposing to arrhythmias. Sprouty proteins are negative regulators of receptor tyrosine kinase signaling, with sprouty-1 acting as an inhibitor of the cardioprotective ERK pathway and regulating p38-signaling. However, its role in cardiac fibroblast function and myocardial fibrosis remains unclear.

Aim

This study aims to investigate the function of sprouty-1 in myocardial fibrosis and heart failure using both in vivo and in vitro models.

Methods

To achieve this, we utilized TCF21-driven MerCreMer Spry1fl/fl mice to silence sprouty-1 specifically in human cardiac fibroblasts. At 8–12 weeks of age, tamoxifen (40 mg/kg, i.p.) was administered once in every two days to induce sprouty-1 deletion. One week later, mice were subjected to thoracic aortic constriction (TAC) for five weeks to induce hemodynamic pressure overload. To target newly formed fibroblasts, tamoxifen was continuously administered orally (20 mg/kg/d in peanut butter). Control Spry1fl/fl mice were similarly treated. Cardiac function was assessed via echocardiography, and heart tissue samples were subjected to histological and molecular biology analyses. Additionally, single-nucleus RNA sequencing was performed to characterize the fibroblast-specific role of sprouty-1 in the diseased heart. In vitro, human cardiac fibroblasts were manipulated using lentiviral-mediated sprouty-1 silencing or overexpression to determine its impact on fibrotic responses. TGFβ1 was used to activate fibroblasts and to induce collagen production.

Results

We find that fibroblast-specific deletion of sprouty-1 attenuates TAC-induced left ventricular hypertrophy and mitigate fibrotic areas. Furthermore, RNA sequencing shows that sprouty-1 attenuates the TAC-induced activation of fibrosis-related genes, including collagen I and connective tissue growth factor (CTGF). Preliminary data from single-nucleus RNA sequencing analyses (N=2 per group) identified 176 differentially expressed (DE) genes in cardiomyocytes, 237 DE genes in fibroblasts and 164 DE genes in endothelial cells. Gene enrichment analysis of DE genes in fibroblasts indicates regulation of TGFβ1 signaling pathway as well as regulation of BMP, FGF and VEGF signaling pathways. In vitro studies in human cardiac fibroblasts indicate that overexpression of sprouty-1 induces collagen production, whereas targeting sprouty-1 attenuates TGFβ1-induced activation of fibroblasts.

Conclusions

These results suggest that sprouty-1 in fibroblasts plays a crucial role in regulating cardiac remodeling and fibrosis. Its deletion mitigates the fibrotic response to pressure overload, highlighting sprouty-1 as a potential therapeutic target for preventing adverse myocardial remodeling in heart failure. Further studies are needed to pinpoint the signaling pathways regulated by sprouty-1 in fibroblasts.

Presentation time
12.05–12.15

MD Henri Kesti
University of Turku

Performance of the academic research consortium for high bleeding risk criteria in ST-elevation myocardial infarction. Significance of smoking as an additional bleeding risk factor

Henri Kesti, University of Turku, Kalle Mattila, Turku University Hospital; Samuli Jaakkola, Turku University Hospital; Joonas Lehto, Turku University Hospital; Nea Söderblom, University of Turku; Kalle Kalliovalkama, University of Turku; Pekka Porela, Turku University Hospital

Aim

The Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria are recommended by guidelines for bleeding risk assessment in ST-elevation myocardial infarction (STEMI). Possible risk factors not included in the criteria are rarely considered. The aim of the present study was to assess which individual ARC-HBR criteria are independent bleeding predictors among STEMI and identify possible other bleeding risk factors.

Methods

Consecutive STEMI patients managed in a Finnish tertiary hospital between 2016-2022 were identified using a database search. Data collection was done by reviewing electronic patient records. Bleeding risk was assessed according to the ARC-HBR criteria. The primary endpoint was non-access site bleeding academic research consortium type 3 or 5 bleeding (major bleeding) during 1-year follow-up. The endpoints were gathered by patient record review and fatal bleeding events occurring outside healthcare facilities from death certificates. Independent bleeding predictors were identified using multivariable competing risk regression analysis.

Results

Of the 1548 analysed STEMI patients, 661 (42.7%) were at high bleeding risk (HBR). The HBR group had an increased bleeding risk but after adjustment only 4 individual ARC-HBR criteria remained associated with bleeding. Smoking status and an increase in white blood cell count were other significant risk factors. Compared with never smokers, current smokers had 3-fold increased bleeding risk (hazard ratio [HR] 3.01, 95% confidence interval [CI] 1.62-5.61) and former smokers 2-fold increased risk (HR 1.99, CI 1.19–3.34). The results were consistent in a sensitivity analysis including only primary percutaneous coronary intervention treated patients. Current smoking fulfilled the ARC-HBR prerequisites for a major bleeding risk criterion. Therefore, by definition current smokers should be considered HBR. The prevalence of current smoking was 16.6% (n = 110) among the HBR group and notably, 40.4% (n = 358) among the non-HBR group.

Conclusions

Current and former smoking predicts major bleeding complications and current smoking is highly prevalent among those classified as non-HBR according to the ARC-HBR criteria. Thus, guideline recommended bleeding risk assessment may fail to identify a large group of patients who are at HBR.

Presentation time
12.05–12.15

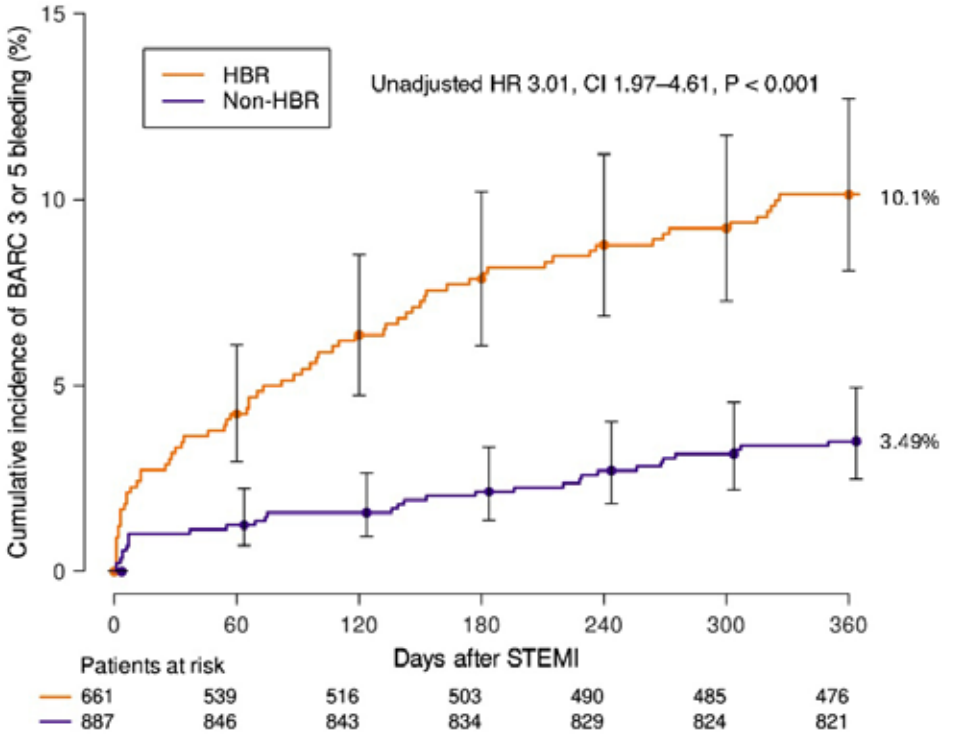
MD Henri Kesti
University of Turku

Table 1. Multivariable Fine-Gray regression model for 1-year BARC 3 or 5 bleeding.

Variable	HR	95% CI	p-value
Age ≥ 75 years*	2.36	1.38–4.03	0.002
OAC*	1.47	0.75–2.86	0.260
GFR 30-59.99 ml/min*	1.63	1.02–2.61	0.040
Haemoglobin < 110 g/L*	1.96	1.06–3.63	0.031
Prior bleeding (major criterion)*	1.88	0.71–4.99	0.210
Active malignancy*	3.11	1.57–6.15	0.001
Smoking	-	-	<0.001
Current§	3.01	1.62–5.61	<0.001
Former#	1.99	1.19–3.34	0.009
White blood cell count (1×10^9/L)	1.03	1.00–1.07	0.031
DAPT-duration$	-	-	0.280
PPI	1.50	0.98–2.29	0.060

*Academic Research Consortium for High Bleeding Risk criterion
§Former smoking excluded (current vs. never)
#Current smoking excluded (former vs. never)
$Categories: no DAPT (reference), < 3 months, 3-5.9 months, 6-9 months, 12 months. HR and CI for category comparisons not provided because the variable was not significant.
In the model: Individual significant (Univariable Fine-Gray p <0.05) ARC-HBR criteria and other significant variables. If both major and minor criterion of the same variable was significant, major criterion was included.
BARC, Bleeding Academic Research Consortium; HR, hazard ratio; CI, confidence interval; OAC, oral anticoagulant; GFR, estimated glomerular filtration rate (CKD-EPI formula); Active malignancy, diagnosis within 12 months prior to index hospitalization or ongoing treatment; DAPT, dual antiplatelet therapy; PPI, proton pump inhibitor.
Modified from Table 3 of Kesti et al. Performance of the ARC-HBR criteria in ST-elevation myocardial infarction. Significance of smoking as an additional bleeding risk factor. Eur Heart J Qual Care Clin Outcomes. 2024 Nov 30:qcae104. Epub ahead of print. (Footnote text modified) (Reproduced under CC BY licence)

Figure 1. Cumulative incidence of BARC 3 or 5 bleeding according to bleeding risk status



BARC, bleeding academic research consortium; HBR, high bleeding risk; HR, hazard ratio; CI, 95% confidence interval; STEMI, ST-elevation myocardial infarction. HR and CI derived from univariable Fine-Gray regression. Modified from Figure 1 of Kesti et al. Performance of the ARC-HBR criteria in ST-elevation myocardial infarction. Significance of smoking as an additional bleeding risk factor. Eur Heart J Qual Care Clin Outcomes. 2024 Nov 30:qcae104. Epub ahead of print. (Text annotations added: HR, CI, P-value, incidences) (Reproduced under CC BY licence)

Presentation time
12.15–12.25

Specialist in pediatrics, MD Alma Kormi
Helsinki University Hospital

CMR hemodynamic risk factors for liver cirrhosis: Insights from the Finnish National Fontan Cohort

Alma Kormi, Helsinki University Hospital, Laura Martelius, Helsinki University Hospital; Sabina Ericsson, Helsinki University Hospital; Ilkka Mattila, Helsinki University Hospital; Tiina Ojala, Helsinki University Hospital

Aim

In Finland, approximately 200 patients with Fontan circulation have reached adulthood, while an estimated 150 children are still on their way to adulthood. As survival rates continue to improve in the Fontan population, the burden of long-term complications, including liver dysfunction, has become increasingly recognized. The pathophysiology of Fontan-associated liver disease (FALD) is complex, with a disease spectrum from hepatic congestion and fibrosis to cirrhosis and hepatocellular carcinoma. Given the absence of a definitive treatment, optimizing hemodynamics remains central to mitigating hepatic injury. Cardiac magnetic resonance (CMR) imaging has emerged as a valuable tool for assessing Fontan hemodynamics and may play a role in risk stratification and early detection of liver disease. This study aimed to identify hemodynamic risk factors from cardiac magnetic resonance (CMR) and clinical data associated with liver cirrhosis in a nationwide cohort of pediatric Fontan patients.

Methods

This retrospective national cohort study included 129 pediatric patients with an extracardiac total cavopulmonary connection (TCPC) who underwent CMR at the New Children's Hospital in Helsinki between February 2019 and September 2024, as part of a standardized follow-up protocol. Liver cirrhosis was diagnosed by liver MRI. Hemodynamic data were obtained from CMR, while clinical and laboratory parameters were retrieved from electronic patient records. SpO2 and peripheral venous pressure (PVP) were assessed from the cubital vein before CMR examination.

Results

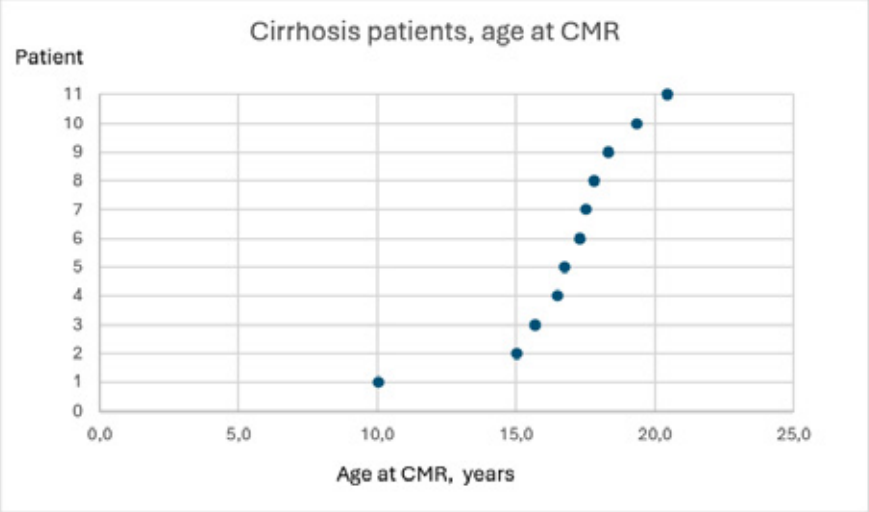
Liver cirrhosis was identified in 11 patients (8.5%), focal nodular hyperplasia in 12 patients (9.3%), and hepatocellular carcinoma in one 8-year-old patient, with a patent ductus venosus noted as a likely predisposing factor. The prevalence of cirrhosis increased with age (Figure). Key factors strongly associated with liver cirrhosis included a systemic right ventricle, CMR-derived McGoon ratio, PVP, and narrowing of the TCPC tunnel. ROC analysis identified a cut-off risk value of 1.8 for the CMR-derived McGoon ratio and 15 for PVP, respectively (Table).

Conclusions

Liver MRI, now widely adopted in Fontan follow-up protocols based on recent consensus recommendations, plays a vital role as the prevalence of liver cirrhosis increases with age in Fontan patients, as observed in our cohort. We identified strong associations between liver cirrhosis and the CMR-derived McGoon ratio (≤1.8), TCPC tunnel narrowing, elevated peripheral venous pressure (≥15 mmHg), and the presence of a systemic right ventricle. These findings highlight the critical importance of optimizing Fontan circulation to slow the progression of FALD and enhance long-term outcomes in this vulnerable population.

Presentation time
12.15–12.25

Specialist in pediatrics, MD Alma Kormi
Helsinki University Hospital



Risk Factors for Liver Cirrhosis in the Finnish National Pediatric Fontan Cohort (n = 129)

Variable	Mean [SD]/ Median (IQR)	p- value	Cutoff (ROC-analysis)	Sensitivity	Specificity
Age at MRI (years)	13.1 [4.3]	<0.001			
RV Morphology		0.013			
CMR McGoon Ratio	1.7 [0.56]	0.003	≤ 1.8	0.82	0.65
Fontan Conduit area (cm^2/m^2)	2.04 (0.27)	0.012	1.1	0.82	0.80
PVP (mmHg)	14.1 [3.3]	0.029	≥ 15	0.73	0.58

McGoon ratio = (LPA diameter at hilus + RPA diameter at hilus) / Descending aorta diameter at diaphragm level. PVP= Peripheral venous pressure, RV= Right ventricle functioning as the systemic ventricle.

Mitochondrial DNA in blood cells and its implications for cardiovascular diseases in a 30-year longitudinal study

Attila Sebe, University of Oulu, Jari Jokelainen, University of Oulu; Juulia Lautaoja-Kivipelto, University of Oulu; Karri Parkkila, University of Oulu; Eija Pirinen, University of Oulu and Oulu University Hospital; Olavi Ukkola, University of Oulu and Oulu University Hospital

Aim

Atherosclerotic cardiovascular diseases remain a major cause of death and morbidity in the rapidly aging Western populations. However, the associated tissue changes may develop over decades before the disease or its risk factors become apparent. Recently, the mitochondrial DNA (mtDNA) amount of peripheral blood cellular components has emerged as a promising molecular marker for aging-related morbidity. Mitochondria are critical for cardiovascular energy homeostasis, but they also regulate oxidative stress, cell death, and metabolite biosynthesis across all tissues. The amount of mtDNA is one of the surrogates of mitochondrial function. Studies have garnered increasing attention due to its association with cardiovascular diseases, related clinical conditions, and occasionally mortality. Nevertheless, results across such studies have proven inconsistent so far. This research aims to enhance the understanding of blood mtDNA quantification as a clinical biomarker, with particular emphasis on cardiovascular health.

Methods

Our distinctive OPERA-cohort (Oulu Project Elucidating Risk of Atherosclerosis) in Finland comprises 1045 individuals initially assessed in the 1990s and subsequently followed for over three decades, including a second visit in the 2010s. Due to the longitudinal nature of this study we have the opportunity to combine clinical and epidemiological data with mtDNA quantification at two distinct time points separated by 20 years. The extensive follow-up period of over 30 years enables the identification of potential biomarkers within a timeframe suitable for effective primary prevention. We used real-time quantitative polymerase chain reaction (qRT-PCR), the 'gold standard' technique, for mtDNA quantification from peripheral blood cellular components.

Results

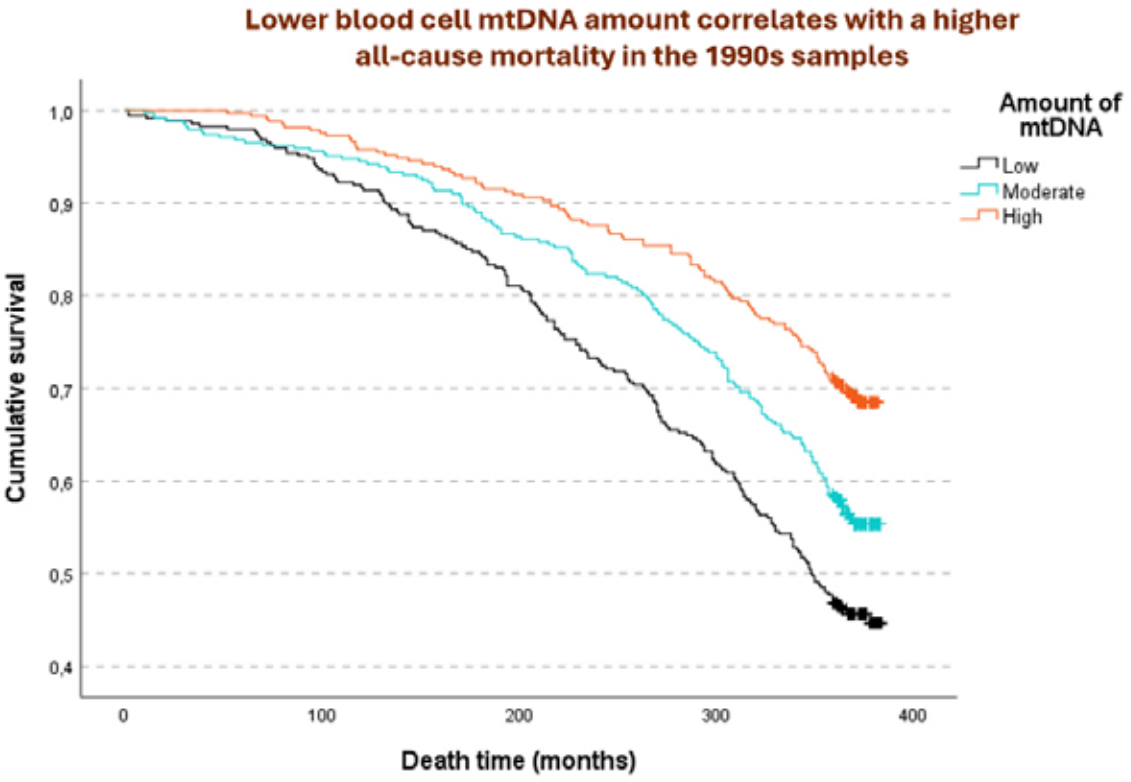
Our study found that lower mtDNA levels in the 1990s blood samples were significantly associated with increased all-cause mortality ($p<0.001$) assessed up to the end of 2022. This trend persisted in a subset analysis of 597 participants from our 2010s follow-up cohort ($p=0.002$). Cardiovascular diseases and cancer were the two main causes of death at both time points. Cox regression analysis of the 1990s samples, accounting for significant covariates, confirmed the association of mtDNA levels with all-cause mortality ($p=0.001$). Additionally, the assessment of all cardiovascular events registered in our hospital database up to 2014 revealed significant association with lower mtDNA levels in the 1990s blood samples ($p<0.001$). Notably, population-level analyses revealed that individuals with lower baseline mtDNA values tend to maintain lower levels over time.

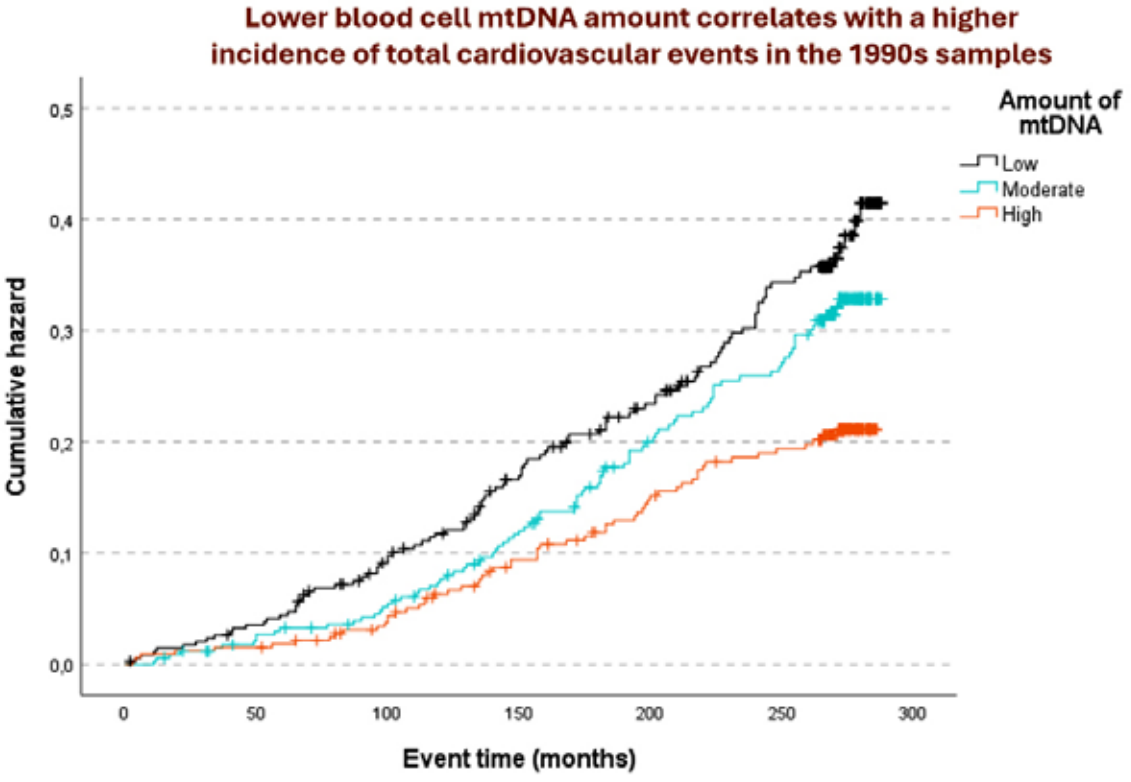
Conclusions

These findings underscore mtDNA's potential as an early biomarker for the development of cardiovascular diseases and may have broader implications for understanding age-related morbidity and mortality risks.

Presentation time
12.25–12.35

Anaesthesiology and Intensive Care Specialist
MD Attila Sebe, University of Oulu





Presentation time
12.35–12.45

Doctoral Candidate Erika Atencio Herre
University of Turku

Activated macrophage folate receptor beta as a diagnostic and therapeutic target in experimental autoimmune myocarditis

Erika Atencio Herre, University of Turku, Arghavan Jahandideh, University of Turku; Wail Nammas, Turku University Hospital; Xiang-Guo Li, University of Turku; Jenni Virta, University of Turku; Heidi Liljenbäck, Turku PET Centre; Jesse Ponkamo, University of Turku; Xiao-Qing Zhuang, Turku PET Centre; Putri Andriana, University of Turku; Madduri Srinivasarao, Purdue University; Philip Low, Purdue University; Yingjuan Lu, Endocyte, Inc.; Juhani Knuuti, Turku University Hospital; Anne Roivainen, Turku University Hospital; Antti Saraste, Turku University Hospital

Aim

Folate receptor-β (FR-β) is expressed on activated macrophages in inflammatory conditions, including cardiac sarcoidosis, and can be targeted for non-invasive detection by aluminum fluoride-18-labeled 1,4,7-triazacyclononane-N,N′,N″-triacetic acid conjugated folate (^{18}F-FOL) positron emission tomography (PET). A new anti-inflammatory therapeutic approach targets the FR-β expressing macrophages using a folate-aminopterin conjugate (EC2319). We evaluated the effects of EC2319 intervention and ^{18}F-FOL PET as a tool to monitor inflammatory activity in a rat model of autoimmune myocarditis.

Methods

Autoimmune myocarditis was induced in male Lewis rats via immunization with porcine cardiac myosin. A group of rats (n=23) were randomized to receive subcutaneous injections of either EC2319 or saline from the beginning of immunization and studied after 21 days. Another group of rats (n=22) with active myocardial inflammation based on ^{18}F-FOL PET after the immunization on day 14, were randomized to receive subcutaneous injections of either EC2319, saline, or TNF-α inhibitor (Etanercept). After 2 weeks (end of treatment), myocardial inflammation was studied by ^{18}F-FOL PET (maximum standardized uptake value = SUVmax) and histology.

Results

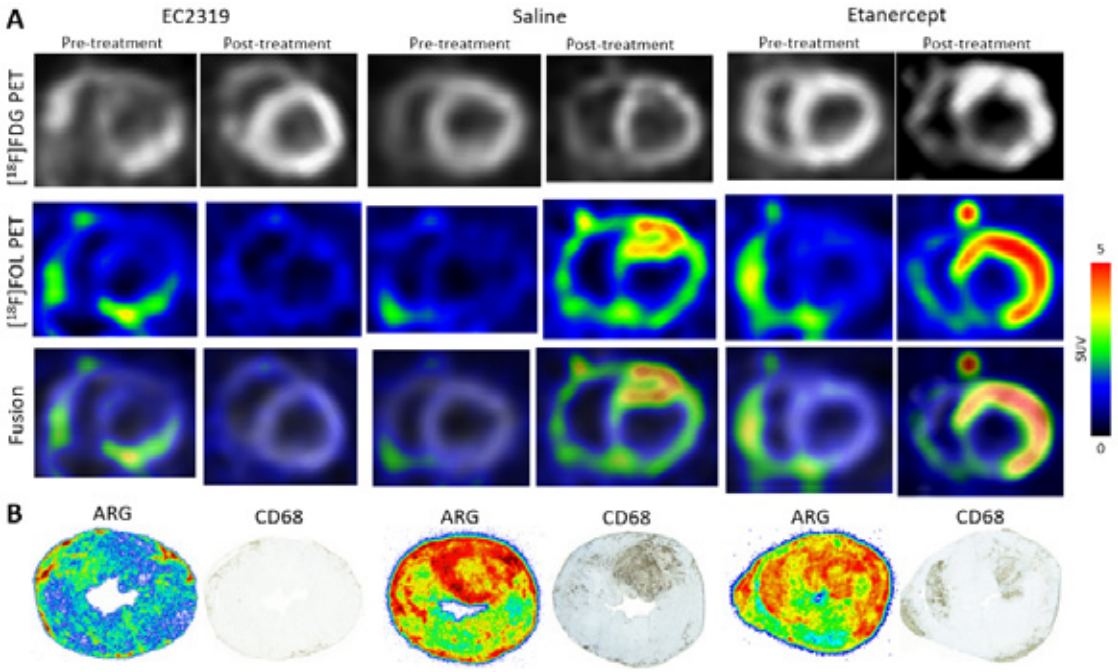
Immunization resulted in decrease in left ventricular ejection fraction (p=0.027 vs. before immunization) and development of myocardial inflammation, which was reduced by EC2319 administered from the beginning of immunization (area of CD68-positive macrophages 4.81±2.94 vs.1.24±0.63%, p<0.001). After immunization, ^{18}F-FOL PET showed increased myocardial tracer uptake indicating active inflammation (SUVmax 1.66±0.31 vs. 1.62±0.25 vs. 1.85±0.50, p=0.893 between EC2319, saline and Etanercept groups, respectively). At the end of treatment, ^{18}F-FOL PET showed lower myocardial tracer uptake after treatment with EC2319 than saline or Etanercept (SUVmax 1.07±0.22 vs. 2.38±0.90 vs. 2.59±0.56, p<0.001). ^{18}F-FOL PET SUV correlated with areal percentage of CD68-positive macrophages (r=0.495, p=0.019), which was lower after treatment with EC2319 than saline or Etanercept (1.04±0.44 vs. 4.15±2.28 vs. 5.66±4.11, p=0.008).

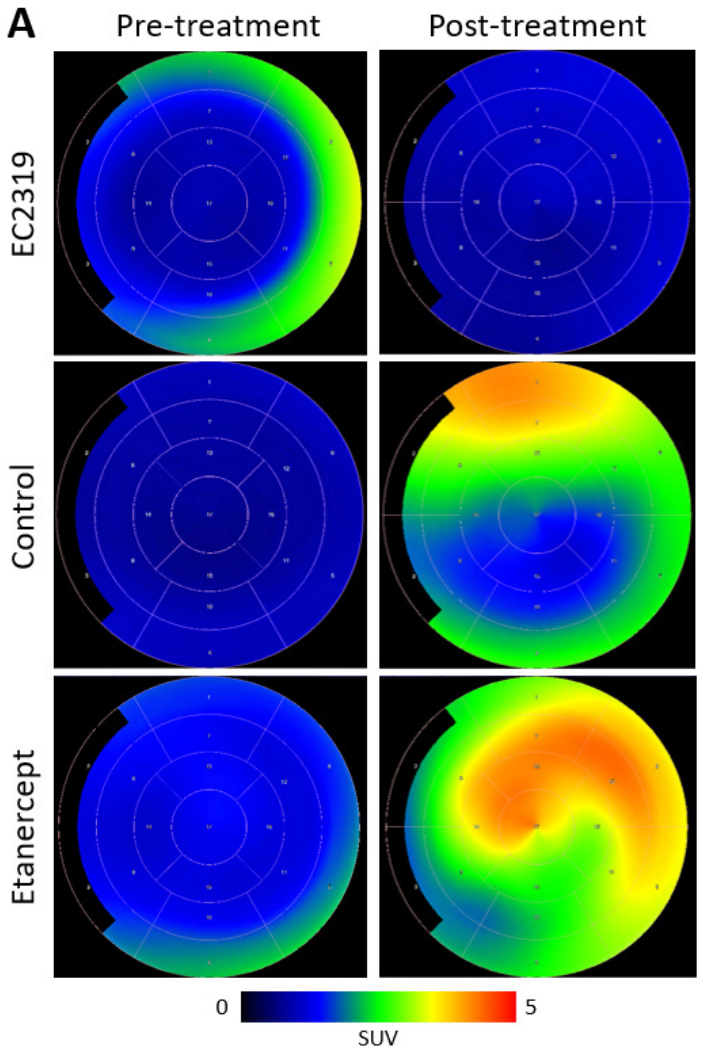
Conclusions

Treatment with EC2319 decreases myocardial inflammation in a rat model of autoimmune myocarditis, indicating that FR-β plays a role in pathogenesis of myocarditis. ^{18}F-FOL PET enables monitoring myocardial inflammatory activity.

Presentation time
12.35–12.45

Doctoral Candidate Erika Atencio Herre
University of Turku





Presentation time
12.45–12.55

BMed Eero Turkkila
University of Oulu

A randomized weight loss trial on a digital health behavioural change support system: Changes in cardiovascular disease risks

Eero Turkkila, University of Oulu, Heta Merikallio, University of Oulu; Marko Merikukka, Oulu University Hospital; Markku Savolainen, University of Oulu; Laura Heikkilä, University of Oulu; Harri Oinas-Kukkonen, University of Oulu; Tuire Salonurmi, University of Oulu; Anna-Maria Teeriniemi, University of Oulu and Oulu University Hospital; Terhi Jokelainen, Oulu University Hospital; Janne Hukkanen, University of Oulu

Aim

Obesity is a risk factor for cardiovascular diseases (CVD). The health behaviour change support system (HBCSS) is a web-based application, that utilizes persuasive systems design (PSD) and methods of cognitive behavioural therapy (CBT) to treat patients living with overweight and obesity. The main objective is to determine the impact of HBCSS on CVD risk using risk calculators.

Methods

In total, 532 participants with overweight or obesity (BMI 27–35 $kg*m^{-2}$) were split into three groups with different intensities of intervention: CBT-based group counselling, self-help guidance (SHG), and usual care. These groups were further divided into HBCSS and non-HBCSS groups. The HBCSS was a 52-week program. At the end of the HBCSS intervention, the participants' 10-year CVD risk was assessed with the FINRISK calculator. The changes were compared between HBCSS and non-HBCSS groups in the participants with obesity. Missing values were replaced with baseline values.

Results

The mean 10-year overall CVD risk at baseline was 3.79 % (SD 3.41 %) in HBCSS group (n = 138) and 3.28 % (SD 3.13 %) in non-HBCSS group (n = 140) with p = 0.194 between groups. After one year, for participants with obesity at baseline, the mean change (percentage points, pp) in 10-year overall risk, was −0.39 (95 % CI −0.59 to −0.20, p < 0.001) in the HBCSS group (n = 138) and −0.15 (95 % CI −0.31 to 0.02, p = 0.086) in the non-HBCSS group (n = 140), with a p-value of 0.059 between groups. For coronary artery disease (CAD) risk, the mean change (pp) was −0.30 (95 % CI −0.46 to −0.14, p < 0.001) in the HBCSS group and −0.10 (95 % CI −0.23 to 0.03, p = 0.139) in the non-HBCSS group, with p = 0.050 between groups. For stroke risk, the mean change (pp) was −0.11 (95 % CI −0.16 to −0.05, p < 0.001) in the HBCSS group and −0.05 (95 % CI −0.11 to 0.00, p = 0.065) in the non-HBCSS group, with p = 0.199 between groups.

Conclusions

Among the participants with obesity, in the HBCSS group, the 10-year risks of overall CVD, CAD, and stroke decreased significantly, while in the controls, the change was not significant. For CAD risk, there was a significant difference between groups favoring the HBCSS. In addition to offering a scalable weight loss solution, our findings suggest that HBCSS may lower the risk of CVD, especially the risk of CAD, in patients living with obesity.

Presentation time
12.55–13.05

MSc Putri Andriana
Turku PET Centre, University of Turku

Targeting anti-inflammatory macrophages via mannose receptor for positron emission tomography imaging of immune response after acute myocardial infarction

Putri Andriana, Turku PET Centre, University of Turku, Senthil Palani, Turku PET Centre, University of Turku; Heidi Liljenbäck, Turku PET Centre & Turku Center of Disease Modeling, University of Turku; Imran Iqbal, Turku PET Centre, University of Turku; Vesa Oikonen, Turku PET Centre, University of Turku; Jenni Virta, Turku PET Centre, University of Turku; Konstantina Makrypidi, Institute of Nuclear and Radiological Science and Technology, Energy and Safety; Johan Rajander, Turku PET Centre, Accelerator Laboratory, Åbo Akademi University; Erika Herre, Turku PET Centre, University of Turku; Aino Suni, Turku PET Centre, University of Turku; Sirpa Jalkanen, MediCity Research Laboratory & InFLAMES Research Flagship, University of Turku; Juhani Knuuti, Turku PET Centre & InFLAMES Research Flagship, University of Turku; Luisa Martinez-Pomares, School of Life Sciences, University of Nottingham; Ioannis Pirmettis, Institute of Nuclear and Radiological Science and Technology, Energy and Safety; Xiang-Guo Li, Turku PET Centre, InFLAMES Research Flagship, University of Turku; Antti Saraste, Turku PET Centre & Heart Center, University of Turku & Turku University Hospital; Anne Roivainen, Turku PET Centre & InFLAMES Research Flagship, University of Turku

Aim

The inflammatory response following myocardial infarction (MI) is a natural innate and adaptive immune function aimed at cardiac recovery and orchestrated by immune cells, including macrophages. Anti-inflammatory (M2) macrophages are a key factor in promoting the process of inflammation resolution and cardiac repair. In this study, we aimed to evaluate the targeting of anti-inflammatory M2 macrophages via their surface receptor, mannose receptor (CD206), for positron emission tomography (PET) imaging of immune response after experimental acute MI, using a novel fluorinated mannosylated dextran derivative Al[18F]F-NOTA-D10CM (Attachment 1).

Methods

We evaluated the binding specificity of fluorescent NOTA-D10CM to M1/M2-polarized macrophages derived from human blood monocytes using flow cytometry. Then, the binding affinity of Al[18F]F-NOTA-D10CM was measured using CD206+ Chinese hamster ovary (CHO) cells. Feasibility of detecting CD206 after MI was evaluated in rats 3 and 7 days after permanent ligation of the left coronary artery or sham-operation using Al[18F]F-NOTA-D10CM PET, followed by digital autoradiography, histology, and immunostaining of the left ventricular myocardium. [18F]FDG PET was performed 1 day before Al[18F]F-NOTA-D10CM PET to visualize the myocardium and MI, and measure infarct size.

Results

Flow cytometry study revealed specific binding of NOTA-D10CM to M2-macrophages. The binding affinity of Al[18F]F-NOTA-DCM for CD206+ CHO cells was 1.83±0.68 nM. [18F]FDG imaging revealed MI in all rats after coronary ligation (average MI size 31.87%±18.20 of the LV with no significant difference between Day 3 and 7,P=0.282). In vivo PET and ex vivo autoradiography showed significantly higher Al[18F]F-NOTA-DCM uptake in the MI area than in remote areas, or the myocardium of sham-operated rats. There was no difference in uptake in the MI area on Day 3 and 7 (Figure 1 and 2). Al[18F]F-NOTA-DCM uptake in the MI area correlated positively with the CD206 staining (r=0.481, P=0.006) (Figure 2).

Presentation time
12.55–13.05

MSc Putri Andriana
Turku PET Centre, University of Turku

Conclusions

Targeted imaging of anti-inflammatory macrophages via mannose receptor using Al[18F]F-NOTA-D10CM PET detects immune response after ischemic myocardial injury, and may be a suitable biomarker for detecting M2-type macrophages during the inflammation resolution process post-MI.

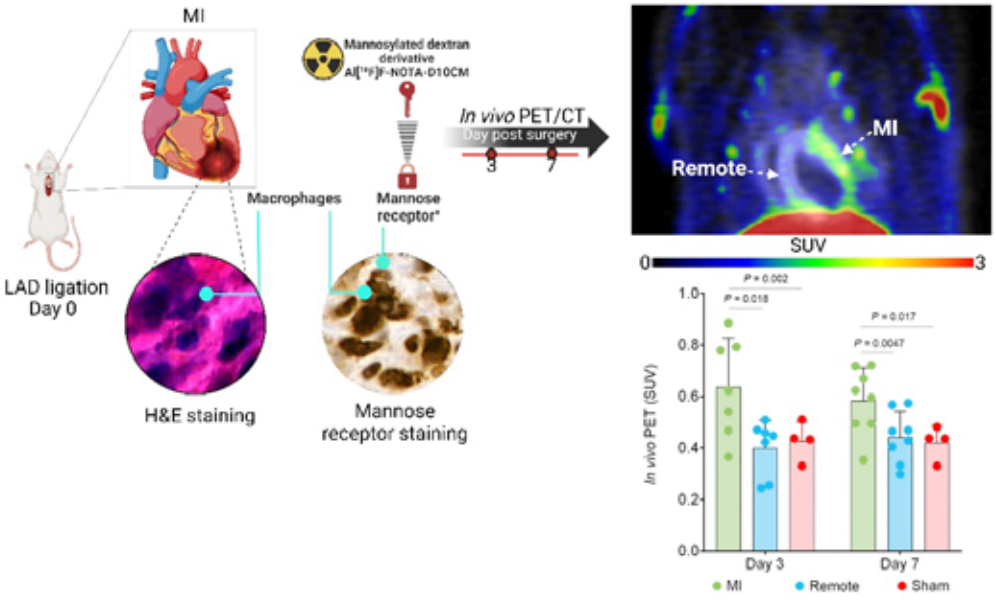


Figure 1. Rats underwent permanent left anterior descendent (LAD) coronary artery ligation to induce myocardial infarction (MI), or sham operation. The ability of the macrophage mannose receptor-targeted positron emission tomography (PET) tracer Al[^{18}F]F-NOTA-D10CM, a mannosylated dextran derivative, to detect inflammatory changes in the myocardium was investigated 3 and 7 days post-surgery. Al[^{18}F]F-NOTA-D10CM showed significantly higher uptake in the MI area compared with the remote area or the myocardium of sham-operated rats.

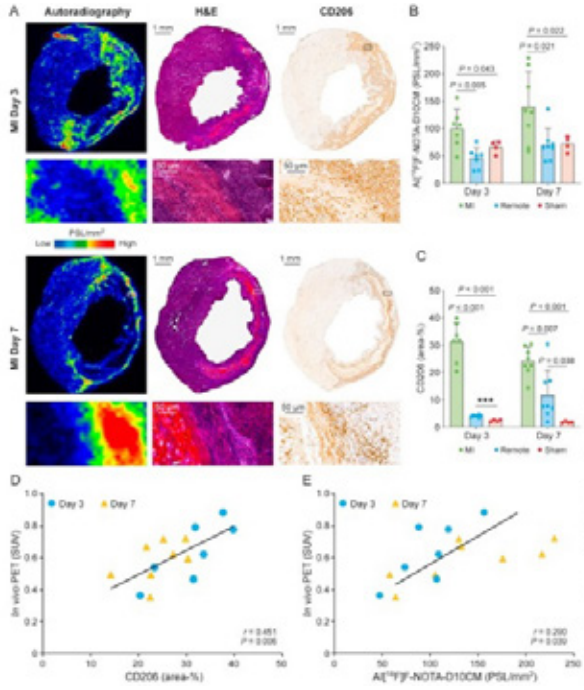


Figure 2. (**A**) Representative Al[^{18}F]F-NOTA-D10CM autoradiographs, and H&E and CD206 staining of the rat LV on Day 3 and 7 post-MI. Quantification of (**B**) Al[^{18}F]F-NOTA-D10CM autoradiography and (**C**) CD206 staining reveals significantly higher signals in the infarcted and border zone areas on both Day 3 and 7 post-MI. Correlation between *in vivo* Al[^{18}F]F-NOTA-D10CM PET results for the MI area and (**D**) the CD206$^+$ area-% or (**E**) *ex vivo* autoradiography on Day 3 and 7 post-MI. PSL/mm^2, photostimulated luminescence per square millimeter.

Meeting is supported by unrestricted educational grant from Boehringer Ingelheim.